

EXHIBIT D
Chronology of Significant Activities Regarding IND 36,704 and NDA 21-272 for
Remodulin™ (treprostinil sodium) Injection

| Date | IND/NDA | Sponsor | Description |
|--------------------|---------|---------------------|---|
| April 15, 1991 | IND | Burroughs Wellcome | Original IND Application |
| August 15, 1991 | IND | Burroughs Wellcome | Protocol 01 Amendment |
| August 23, 1991 | IND | Burroughs Wellcome | Investigator CV and 1572 Protocol 01 |
| October 28, 1991 | IND | Burroughs Wellcome | Investigator CV and 1572 Protocol 01 |
| October 19, 1992 | IND | Burroughs Wellcome | IND Annual Report |
| December 10, 1993 | IND | Burroughs Wellcome | IND Annual Report |
| April 21, 1994 | IND | Burroughs Wellcome | Request to place IND on Inactive Status |
| February 3, 1997 | IND | LungRx | Letter regarding transfer from Glaxo Wellcome to LungRX, Inc. |
| February 14, 1997 | IND | LungRx | 1 st Submission under LungRx – provides for new Protocol P01:01, Investigator's Brochure, Clinical Report, and CV and 1572 for Dr. Rubin |
| April 15, 1997 | IND | LungRx | CMC update/response to FDA questions, Amendment 1 to P01:01, and Investigators 1572 and CVs |
| June 4, 1997 | IND | LungRx | Orphan designation granted for PPH |
| June 10, 1997 | IND | LungRx | Amendment 2 to P01:01 |
| July 18, 1997 | IND | LungRx | Amendment 3 to P01:01 |
| August 7, 1997 | IND | LungRx | New Protocol P01:02 (PPH), Investigators Badesch, Barst, Brundage, McGoon, Robbins, Rubin and Tapson CVs and 1572s and summary of Toxicology Report on 3-day Rat Infusion |
| September 12, 1997 | IND | LungRx | New Protocol P02:01 (Portopulmonary Hypertension), Investigator Gaine CV and 1572 |
| November 11, 1997 | IND | LRX Pharmaceuticals | Correspondence re: 1) inability to develop assay for 15AU81, and 2) PK analysis for P01:02 |
| November 20, 1997 | IND | LRX Pharmaceuticals | Company Name change, Amendment 1 to P02:01 adding clinical chemistry profile, including liver function tests and Investigator registrations for Drs. Badesch, Frost, Bourge, McLaughlin, and Brundage |
| November 21, 1997 | IND | LRX Pharmaceuticals | Registration of Investigators Bourge, Frost, and Rich |
| December 22, 1997 | IND | LRX Pharmaceuticals | Amendment 1 for P01:02 (PPH) |
| December 23, 1997 | IND | LRX Pharmaceuticals | New Protocol Submission P03:01(Lower Limb Ischemia), Investigator CV and 1572 |
| January 15, 1998 | IND | LRX Pharmaceuticals | Amendment 2 to P02:01, (Portopulmonary Hypertension), modifying exclusion criteria |
| February 2, 1998 | IND | United Therapeutics | Company and Drug Name change, End of Phase II meeting confirmation, Phase III Development Plan |
| February 3, 1998 | IND | United Therapeutics | SAE Report for P01:01 patient 02005 |
| March 13, 1998 | NDA | United Therapeutics | Minutes of the February 20, 1998 meeting between FDA and UT |
| March 16, 1998 | IND | United Therapeutics | Amendment 1 to P03:01(PVD/Lower leg Ischemia), modification to 1571 to provide for Dr. McAllister and Dr. Smith for Safety |
| March 19, 1998 | IND | United Therapeutics | IND Annual Report |
| March 26, 1998 | IND | United Therapeutics | Correspondence re: End of Phase II meeting, request for expedited development for PVD |
| April 7, 1998 | IND | United Therapeutics | Pre-Clinical Toxicology Studies: 3-Day Rat; Acute Dose Study in Rat; 14-Day Dose Study in Rat; Acute Dose Study in Beagle Dogs; 14-Day Dose Study in Beagle Dogs; |
| April 10, 1998 | IND | United Therapeutics | New Protocol Submission P01:03 (PPH 8 Week Study), Investigator Registrations Rich, Barst, Bourge, Gaine, and Shapiro |
| May 12, 1998 | IND | United Therapeutics | Amendment 1 of P01:03, providing for addition of blood sample collection as per FDA suggestion |
| June 17, 1998 | IND | United Therapeutics | Amendment 2 of P01:03, providing for new formulations of drug to be used, for dose administration changes, for a pregnancy test in week 8, for three new patients to be included, for vital signs to be collected |

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| | | | during dose optimization and for AEs to be followed to resolution |
| June 19, 1998 | IND | United Therapeutics | CTX Variation (Clinical Trials Exemption) |
| June 23, 1998 | IND | United Therapeutics | New Protocol P01:06 (Continuation Study), Investigator Registration for Drs. Barst, Bourge, Rich and Gaine |
| July 22, 1998 | IND | United Therapeutics | Amendment 3 of P02:01, providing for modification of entry criteria and UT (company's) address change |
| August 7, 1998 | IND | United Therapeutics | P01:02 New Investigator Registration, Dr. Oudiz to replace Dr. Brundage |
| November 2, 1998 | IND | United Therapeutics | New Protocols P01:04 (North American Pivotal) and P01:05 (ROW Pivotal) includes original revision and Amendment 1, Registration of Investigators, and CMC informational amendment providing for the new formulation of UT-15 to be used in the studies |
| October 26, 1998 | IND | United Therapeutics | Amendment 2 to P01:06, providing to allow an optional hemodynamics and exercise assessment in patients entering this study from P01:03 |
| November 9, 1998 | IND | United Therapeutics | Amendment 2 to P01:04 and P01:05, providing for modification of dose regimen, clarification of inclusion/exclusion criteria and amend statistical analysis section to permit second interim efficacy analysis on combined trial data |
| December 22, 1998 | IND | United Therapeutics | Amendment 3 to P01:04 and P01:05; providing for the modification of several entry criteria; adding a global quality of life instrument as a secondary efficacy measurement; revising the statistical analysis section; and clarifying certain existing study procedures. |
| December 29, 1998 | IND | United Therapeutics | Amendment 3 to P01:06, providing consistency between this uncontrolled study and two controlled studies, specifically; updated information on drug formulations and storage conditions; a revision in dosing regimen; and additional expected adverse events related to UT-15 |
| February 12, 1999 | IND | United Therapeutics | Registration of new P01:05 Investigators for Israeli sites; and registration of P01:06 Investigators |
| April 15, 1999 | IND | United Therapeutics | CMC changes in two volumes, specifically changes to the DS reference standard, synthesis method and analytical controls; DP updated analytical specifications and stability data; and Placebo to include a new specification for metacresol. |
| May 4, 1999 | IND | United Therapeutics | Correspondence requesting meeting regards randomization issues |
| April 30, 1999 | IND | Quintiles | 15-Day IND Safety Report |
| May 5, 1999 | IND | United Therapeutics | IND Annual Report |
| May 7, 1999 | IND | United Therapeutics | Drug Product Stability Strategy and request for conference call to discuss stability |
| May 27, 1999 | IND | United Therapeutics | New Protocol P01:07, for conducting the Bioavailability Study (PK) |
| June 21, 1999 | IND | United Therapeutics | Submission of final pre-clinical toxicology and toxicokinetic study reports, in seven volumes |
| July 7, 1999 | IND | United Therapeutics | Submission includes correspondence regarding 7/15/99 meeting with Agency and two certificates of Analysis for lots UT15-99D002 and UT-15-99E001 |
| July 23, 1999 | IND | United Therapeutics | Submission of P01:08 protocol, Acetaminophen interaction study with Investigator Data & 1572 |
| July 26, 1999 | IND | United Therapeutics | Submission of P01:09 protocol, Chronic PK Study in Health Volunteers with Investigator Data & 1572 |
| August 5, 1999 | IND | United Therapeutics | Submission of 7/15/99 FDA mtg. minutes |
| August 18, 1999 | IND | United Therapeutics | Revised Stability Strategy and additional request for approval of 7/15/99 FDA mtg. minutes |

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| August 20, 1999 | IND | United Therapeutics | Registration of New P01:05 Investigators (North American Sites), CVs & 1572s and Investigator's Brochure |
| September 13, 1999 | IND | United Therapeutics | Information Amendment: Chemistry, Manufacturing and Controls: 10.0 mg/mL; HPLC drug product assay method |
| September 23, 1999 | IND | United Therapeutics | New Investigators for P01:05 |
| September 28, 1999 | IND | United Therapeutics | Request for Clinical/Nonclinical Pre-NDA Meeting |
| September 28, 1999 | IND | United Therapeutics | Request for CMC Pre-NDA Meeting |
| October 13, 1999 | IND | United Therapeutics | Registration of last 04 investigator's into the 05 study; CVs and 1572s |
| October 14, 1999 | IND | United Therapeutics | Orphan Application Request for Designation for PPH |
| October 21, 1999 | IND | United Therapeutics | Pre-NDA CMC Package Submission |
| October 27, 1999 | IND | United Therapeutics | Pre-NDA Clinical/Nonclinical Package |
| November 2, 1999 | IND | United Therapeutics | Orphan Designation Approved |
| November 10, 1999 | IND | United Therapeutics | Amendment 4 to P01:06 providing for Portopulmonary Hypertension and HIV patients |
| December 6, 1999 | NDA | United Therapeutics | Minutes of the November 15, 1999 Pre-NDA meeting between FDA and UT |
| December 7, 1999 | IND | United Therapeutics | Toxicology Submission, 6 month dog continuous subcutaneous infusion of UT-15 |
| December 14, 1999 | IND | Quintiles | 15 Day Safety Report |
| December 13, 1999 | IND | United Therapeutics | Response to CMC pre-NDA meeting minutes |
| January 3, 2000 | IND | United Therapeutics | New Protocol P01:10 (Mass Balance Radio-label Study) and CMC amendment for radio label batch |
| January 6, 2000 | IND | United Therapeutics | New Protocol P01:11 – Compassionate use study in transition from IV Flolan to Subcutaneous UT-15 |
| January 17, 2000 | IND | United Therapeutics | Pre-NDA Clinical-Nonclinical Mtg. Minutes |
| January 19, 2000 | IND | United Therapeutics | Statistical Analysis Plan |
| February 1, 2000 | IND | Quintiles | 15-Safety Report (from Quintiles) |
| February 2, 2000 | IND | United Therapeutics | Carcinogenicity Rationale |
| February 9, 2000 | IND | United Therapeutics | Amendment 5 to P01:06 |
| February 10, 2000 | IND | United Therapeutics | Nonclinical Amendment Toxicology and PK Studies in 4 volumes |
| February 18, 2000 | IND | Quintiles | IND Safety Report SAE Report |
| February 18, 2000 | IND | United Therapeutics | Protocol Amendment Revision to Amendment 5 to P01:06 |
| March 6, 2000 | IND/NDA | United Therapeutics | Statistical Analysis Plan, final review before unblinding |
| March 23, 2000 | IND/NDA | United Therapeutics | Final Statistical Analysis Plan Issues for P01:04 and P01:05 (SER072) |
| April 11, 2000 | NDA | United Therapeutics | Letter regarding exemption from conducting carcinogenicity studies |
| April 17, 2000 | NDA | United Therapeutics | Confirmation of Presubmission of NDA |
| April 28, 2000 | IND | United Therapeutics | 1999-2000 IND Annual Report |
| May 5, 2000 | IND | United Therapeutics | Amendment # 1 to Protocol P01:11 to allow patients to transition to UT-15 from Flolan |
| May 18, 2000 | IND | United Therapeutics | Amendment #6 to Protocol P01:06 to allow thromboembolic patients |
| June 6, 2000 | IND | United Therapeutics | New Protocol P01:12 – Subcutaneous Infusion of UT-15 Therapy on Single-Dose Warfarin Pharmacodynamics and Pharmacokinetics in Healthy Patients. |
| June 29, 2000 | IND | United Therapeutics | IND Safety Report – P01:06 Anaemia, Israel site 57; Patient # 557005 |
| August 11, 2000 | NDA | United Therapeutics | Partial NDA submission - CMC and Item 5 Volumes to FDA (35 total; vol 1.1-1.35) |
| September 26, 2000 | IND | United Therapeutics | New Investigators – P01:11 Nicholas S. Hill, MD; Prof. T.W. Higenbottam; Ronald J. Oudiz, MD; David Dunbar Ivy, MD |
| July 3, 2000 | IND | United Therapeutics | IND Safety Report Follow-up P01:06 Anemia, Patient 557005 |
| October 13, 2000 | NDA | United Therapeutics | Synquest (UT Chicago) Acceptable Inspection notification |

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| October 16, 2000 | NDA | United Therapeutics | Remaining NDA documents submitted to FDA; Vol 2.1 to 2.69 |
| October 16, 2000 | IND/NDA | United Therapeutics | Name change from Uniprost to Remodulin |
| October 19, 2000 | NDA | United Therapeutics | Letter from FDA confirming receipt of NDA on October 16, 2000 |
| October 23, 2000 | NDA | United Therapeutics | Response to FDA request for microbiology information |
| October 25, 2000 | IND | United Therapeutics | Registration of New Investigators of P01:06 Study (Zwicke; Lawrence) |
| October 31, 2000 | IND | United Therapeutics | IND Safety Report |
| November 3, 2000 | NDA | United Therapeutics | P01:04/05: DSMB and Steering Committee Summary results |
| November 10, 2000 | NDA | United Therapeutics | P01:04/05: Information requested for statistician |
| November 10, 2000 | NDA | United Therapeutics | Response to FDA request. List of microbial deficiencies provided. |
| November 13, 2000 | NDA | United Therapeutics | P02:01: Information for Dr. Nguyen and water injection diagram |
| November 16, 2000 | NDA | United Therapeutics | Information for clinical sites 02 (Barst), 09 (Frost) and 10 (Bourge) |
| November 16, 2000 | NDA | United Therapeutics | CRFs requested by Dr. Stockbridge P01:04: 23002 and 09001 P01:05: 50013 |
| November 28, 2000 | IND | United Therapeutics | IND Safety Report |
| November 30, 2000 | IND | United Therapeutics | IND Safety Report |
| November 30, 2000 | IND | United Therapeutics | IND Safety Report |
| November 30, 2000 | IND | United Therapeutics | IND Safety Report |
| December 1, 2000 | NDA | United Therapeutics | P01:06: Interim Study Updated for Volume 2.51 of the NDA submitted September 15, 2000, page 13789, lab data |
| December 1, 2000 | IND | United Therapeutics | Registration of New Investigators of P01:06 Study (Waxman, Edelman, Granton, Shardonofsky) |
| December 4, 2000 | NDA | United Therapeutics | CMC Background information for the December 7, 2000 meeting |
| December 7, 2000 | NDA | United Therapeutics | CMC: December 7 th minutes and response regarding starting materials for the API synthesis |
| December 14, 2000 | NDA | United Therapeutics | Correspondence regarding not presenting to the Cardio Renal Drug Products Committee in February Advisory Committee |
| December 22, 2000 | NDA | United Therapeutics | Response to FDA request – Starting materials for API synthesis. |
| December 22, 2000 | NDA | United Therapeutics | CMC: Updated Stability Data for 10 mg/mL strength |
| January 4, 2001 | IND | United Therapeutics | Registration of New Investigator of P01:06 Study (Ross) |
| January 5, 2001 | NDA | United Therapeutics | Letter to request meeting on January 25, 2001 to discuss clinical issues |
| January 5, 2001 | NDA | United Therapeutics | Response to FDA request – Classification of 18 discontinued patients in P01:04/05 |
| January 11, 2001 | NDA | United Therapeutics | Additional information on patients in P01:04/05 Pivotal Studies regarding discontinuations due to AEs |
| January 18, 2001 | IND | United Therapeutics | IND Safety Report |
| January 23, 2001 | NDA | United Therapeutics | Agenda and package for the January 25, 2001 Clinical and PK meeting with FDA |
| January 25, 2001 | NDA | United Therapeutics | Submission of P01:12 |
| February 2, 2001 | MAA | United Therapeutics | MAA submitted |
| February 2, 2001 | IND | United Therapeutics | Registration of New Investigators P01:06 (Gibbs) |
| February 2, 2001 | NDA | United Therapeutics | Response to Steering Committee queries and January 25, 2001 call with Dr. Karkowsky |
| February 6, 2001 | NDA | United Therapeutics | Final Minutes of January 25, 2001 meeting between FDA and UT |
| February 9, 2001 | NDA | United Therapeutics | Call from Dr. Karkowsky requesting information and clarification on several issues |
| February 15, 2001 | NDA | United Therapeutics | Response to request for information regarding the January 25 th meeting. Telephone conversation with Dr. Karkowsky on February 9, 2001 for additional information to complete the review. |
| February 15, 2001 | NDA | United Therapeutics | 120-Day Safety Update (Volumes 3.1 to 3.12) |
| February 15, 2001 | NDA | United Therapeutics | Response to FDA request for information. SAS Data Sets for Safety |

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| | | | Update for P01:06 on CD for 120-Day Safety Report Update. Hardcopy of annotated CRFs also enclosed |
| February 19, 2001 | NDA | United Therapeutics | Response to FDA request for information. Microbial deficiencies regarding the 11/6/00 letter. Reference to 11/10/00 response to issues. Telephone conversation with Drs Langille and Cooney on 2/1/01. Telephone conversation regarding hand stoppering of vials (from 11/10/00 response). |
| February 23, 2001 | NDA | United Therapeutics | Response to FDA request for information. CMC Amendment of updated stability |
| February 23, 2001 | IND | United Therapeutics | IND Safety Report Follow-up |
| February 26, 2001 | NDA | United Therapeutics | Diskette and hard copy of draft labeling. Also incorporation of new trade name Remodulin. |
| February 28, 2001 | NDA | United Therapeutics | PK Amendment: Response to FDA request. P01:12 Warfarin Interaction Study tables and listings. |
| February 28, 2001 | NDA | United Therapeutics | CMC Amendment regarding specifications and testing for UT-15. Discussion of changes to drug substance and drug product specifications (97W86; 751W93; 1AU90). |
| March 1, 2001 | NDA | United Therapeutics | CMC Amendment regarding specifications and testing for UT-15. Amendment committing to changes to drug substance and drug product specifications. Also revised test methods of drug substance and drug product specifications |
| March 12, 2001 | NDA | United Therapeutics | Meeting with FDA regarding NDA issues |
| April 4, 2001 | NDA | United Therapeutics | Briefing Document for April 11, 2001 meeting |
| April 9, 2001 | NDA | United Therapeutics | Briefing Document addendum with completers analysis of walk |
| April 11, 2001 | NDA | United Therapeutics | Meeting with FDA regarding analysis of P01:04/05 data combining exercise tolerance with Borg Dyspnea scores |
| April 12, 2001 | NDA | United Therapeutics | Amendment to pending application – additional statistical analyses exercise and Borg Dyspnea scores in P01:04/05 |
| April 12, 2001 | IND | United Therapeutics | IND Safety Report |
| April 24, 2001 | IND | United Therapeutics | Registration of New Investigators of P01:06 Study (Pepke-Zaba, Boonstra) |
| May 9, 2001 | IND | United Therapeutics | P01:06 Amendment 7- Extension of the chronic treatment phase of the study from 3 to 5 years |
| May 14, 2001 | NDA | United Therapeutics | Amendment to pending application - additional analyses provided to support the NDA |
| June 14, 2001 | NDA | United Therapeutics | Amendment to pending application – Nonproprietary name change of Remodulin Injection from treprostinol to treprostinil |
| June 14, 2001 | NDA | United Therapeutics | Amendment to pending application – CMC amendment |
| June 22, 2001 | NDA | United Therapeutics | Meeting with FDA to discuss Benefits-to-Risk profile of Remodulin |
| June 25, 2001 | NDA | United Therapeutics | Amendment to pending application – Follow-up document to outline the Benefits-to-Risk profile of Remodulin |
| July 5, 2001 | NDA | United Therapeutics | NDA withdrawn for resubmission at a later date |
| August 9, 2001 | NDA | United Therapeutics | Cardiovascular and Renal Drugs Advisory Committee recommending approval of Remodulin by a 6-3 vote. NDA resubmitted. |
| August 16, 2001 | NDA | United Therapeutics | Amendment to pending application – additional analyses submitted following advisory committee |
| August 20, 2001 | IND | United Therapeutics | IND Safety Report |
| September 24, 2001 | NDA | United Therapeutics | Amendment to pending application – Further documentation supporting the Benefits-to-Risk profile of Remodulin |
| September 27, 2001 | IND | United Therapeutics | Registration of New Investigator of P01:06 Study (Kiely) |
| September 28, 2001 | IND | United Therapeutics | IND Safety Report |

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| October 2, 2001 | NDA | United Therapeutics | Amendment to pending application – Summary comparison of Remodulin vs Bosentan |
| October 5, 2001 | IND | United Therapeutics | IND Safety Report |
| October 30, 2001 | NDA | United Therapeutics | Request submitted for priority evaluation status of Remodulin |
| November 1, 2001 | NDA | United Therapeutics | Amendment of pending application – submission of USAN "Statement on a Nonproprietary Name Adopted by the USAN Council" |
| November 13, 2001 | IND | United Therapeutics | IND Safety Report |
| December 17, 2001 | IND | United Therapeutics | Annual Report for Feb 2000 to Feb 2001 |
| December 13, 2001 | NDS | United Therapeutics | Canada – New Drug Submission |
| February 8, 2002 | NDA | United Therapeutics | Approvable letter issued for Remodulin |
| February 8, 2002 | IND | United Therapeutics | IND Safety Report |
| February 13, 2002 | NDA | United Therapeutics | Meeting with FDA to discuss Approvable Letter requirements |
| February 13, 2002 | NDA | United Therapeutics | Response to Approvable Letter - Submission of vial and carton labels |
| February 25, 2002 | NDA | United Therapeutics | Submission of postmarketing protocol P01:13 |
| February 28, 2002 | NDA | United Therapeutics | Submission of P01:13 informed consent |
| March 1, 2002 | NDA | United Therapeutics | Request for CMC clarification |
| March 7, 2002 | NDA | United Therapeutics | Meeting with FDA to discuss P01:13 |
| March 14, 2002 | NDA | United Therapeutics | CMC Amendment- updated stability commitment statement |
| March 20, 2002 | NDA | United Therapeutics | Complete Response to Approvable Letter and submission of final printed label (package insert) |
| April 1, 2002 | NDA | United Therapeutics | Class 1 Complete Response Resubmission: Final Response to Approvable Letter |
| April 9, 2002 | NDA | United Therapeutics | CMC Amendment |
| April 19, 2002 | IND | United Therapeutics | Annual Report for Feb 11, 2001 – Feb 10, 2002 and Updated Investigator's Brochure |
| May 21, 2002 | NDA | United Therapeutics | Approval letter issued for Remodulin |